Gemphire Announces Initiation of Phase 2a Clinical Trial of Gemcabene in Pediatric Non-Alcoholic Fatty Liver Disease (NAFLD)

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Pediatric NAFLD/NASH is a large and untreated market; provides an opportunity to advance gemcabene in an underserved area with millions of affected patients

Proof-of-concept clinical trial expands company's differentiated NAFLD/NASH program across both adults and adolescents

US Patent No. US 9,849,104, "Treatment of NASH with Gemcabene" issued, further enhancing intellectual property protection

Company to host conference call and live webcast at 4:30 pm ET today

LIVONIA, Mich., Jan. 31, 2018 (GLOBE NEWSWIRE) -- Gemphire Therapeutics Inc. (NASDAQ:GEMP), a clinical-stage biopharmaceutical company focused on developing and commercializing therapies for cardiometabolic disorders, including dyslipidemia and Nonalcoholic Steatohepatitis (NASH), announced today initiation of a Phase 2a proof-of-concept (POC) clinical trial investigating gemcabene as a treatment for pediatric nonalcoholic fatty liver disease (NAFLD). NAFLD describes a continuum of disease from its mildest form of isolated fat infiltration of the liver, or steatosis, which can progress in severity to NASH, and is the leading cause of chronic liver disease in children and adolescents in the United States. The trial is part of a broader program to develop gemcabene in NAFLD/NASH, and will run in parallel with the recently initiated clinical trial investigating gemcabene in familial partial lipodystrophy (FPL). Top line results from the pediatric NAFLD trial are expected in early 2019.

"We are very excited to initiate this pediatric POC clinical trial as the next step in our program to evaluate gemcabene as a highly differentiated treatment for NAFLD and NASH in both adults and adolescents. We believe gemcabene, based on its favorable safety profile and novel mechanism targeting the underlying pathologies of both dyslipidemia and inflammation, will have a distinct competitive advantage," said Steven Gullans, Ph.D., Interim President and CEO of Gemphire. "Given the paucity of clinical trials in pediatric NAFLD, and the large number of adolescents already identified with this condition, we expect to recruit pediatric patients faster than is currently possible in similar adult trials. We anticipate relatively little competition in this segment of the market over the next several years."

Phase 2a clinical trial (GEM-IIT-601) designed to show clinical proof-of-concept in pediatric NAFLD

The open label trial is expected to enroll approximately 40 adolescent children between the ages of 12 and 17 who are diagnosed with NAFLD and abnormal liver function as assessed by liver transaminases. Patients will receive gemcabene at a dose of 300 mg once daily. The primary endpoint is a measure of the change in serum alanine transaminase (ALT), an enzyme that serves as a biomarker of liver function, from baseline to 12 weeks.

Secondary endpoints include change in hepatic steatosis as measured by non-invasive magnetic resonance imaging – proton density fat fraction (MRI-PDFF), change in liver inflammation and fibrosis (LIF) score by non-invasive MRI liver multiscan, change in AST, insulin sensitivity, serum lipids (including triglycerides), apolipoproteins, and inflammatory markers (including hsCRP) as well as safety and tolerability. Additionally, the company plans to conduct sub-studies evaluating gemcabene's pre- and post-treatment effects on the duration of elevated fat in the blood after a meal, also known as post-prandial lipemia, and measurement of the liver's ability to synthesize triglycerides, also known as *de novo* lipogenesis, each a form of metabolism that is usually elevated in NAFLD patients.

"We are excited to explore the potential of gemcabene in pediatric NAFLD patients with Gemphire and our other investigators," said Miriam Vos, MD, MSPH, Assistant Professor of Pediatrics at the Emory University School of Medicine and Primary Investigator of this study. "Pediatric NAFLD, which often progresses to NASH, is a growing

epidemic and can lead to significant morbidities in these children. When exploring new therapies in children, safety is a major concern and gemcabene's safety profile as demonstrated in nearly 1100 adults provides a strong rationale to initiate this trial in pediatric patients with NAFLD. Additionally, the demonstrated effects of lowering triglycerides, inflammation, hepatic NAFLD Activity Score (NAS), intrahepatic fat and *de novo* lipogenesis in preclinical models, suggest that gemcabene may be beneficial in this patient population."

"We believe that gemcabene has many of the right attributes for clinical success in NAFLD/NASH," said Lee Golden, MD, Chief Medical Officer of Gemphire Therapeutics. "Clinical and preclinical studies suggest it may be both cardio-protective and liver-protective. Gemcabene has been studied in 23 completed clinical trials with nearly 1100 subjects treated, and gemcabene has been observed to have a positive safety profile without significant adverse effects, both as monotherapy and in combination with high dose statins and with metformin, a common therapy for patients with diabetes. Additionally, gemcabene has shown meaningful lowering of triglycerides and atherogenic lipid proteins as well as marked decreases in inflammation, as measured by reductions in C-reactive protein (CRP). When treating NAFLD/NASH it is important to look for therapies that can impact multiple underlying cardiometabolic components of the disease that ultimately lead to progressive inflammation, cell death and fibrosis. Moreover, given the co-morbidities in these patients, drug candidates need to be safe when combined with commonly prescribed medications in these patients, and gemcabene appears to meet this attribute to date."

Pediatric NAFLD/NASH is a major public health crisis affecting millions in the U.S.

Pediatric nonalcoholic fatty liver disease (NAFLD) is a condition called "fatty liver" characterized by excess fat in the liver, but no inflammation or liver damage. NAFLD is a major public health concern given the recent increase in its prevalence and link to obesity and other metabolic comorbidities. NAFLD has emerged as the leading cause of chronic liver disease in children and adolescents in the United States. A two- to three-fold rise in the rates of obesity in children over the last 20 years is likely responsible for the epidemic of NAFLD. It is estimated that 20% of children between the ages 12 to 19 are obese, and 36% of obese children have NAFLD. NALFD is estimated to affect 7 million children overall in the U.S.; the estimated population prevalence for pediatric NASH is 2 million children.

Pediatric NAFLD and NASH, while similar to the adult diseases, have distinct pathophysiological characteristics in terms of histology, disease progression, and ultimately adverse outcomes at early ages. Steatosis and portal inflammation tend to be more severe in pediatric NAFLD. Children diagnosed with NAFLD often have elevated serum lipids and diabetes or prediabetes and have a 13.6 times greater risk of dying over the next 20 years, than children without NAFLD. Progression of NAFLD and NASH can lead to liver fibrosis, cirrhosis, fibrosis, hepatocellular carcinoma, liver failure and liver-related death. It is estimated that 10- 25% of children with NAFLD progress to NASH and then advanced fibrosis/cirrhosis by their third or fourth decade of life. Liver transplantation is currently the only treatment for advanced cirrhosis with liver failure. At this time, there are no approved treatments approved by the FDA for NAFLD or NASH for either adults or children. Current treatment strategies involve lifestyle changes.

Pediatric study is part of a differentiated NAFLD/NASH program at Gemphire

In addition to the pediatric NAFLD study announced today, Gemphire is also evaluating gemcabene for treatment of adult Familial Partial Lipodystrophy (FPL), which is a NASH-related indication. FPL is a rare genetic disorder and orphan disease characterized by an abnormal distribution of body fat, which can lead to a variety of metabolic abnormalities including NASH. Individuals living with FPL face significant medical complications that currently have no FDA approved treatments. The company has initiated a Phase 2a study to assess the efficacy and safety of two dosing regimens of gemcabene in up to eight FPL patients with elevated triglycerides and NAFLD. Top line results are anticipated in late 2018.

Novel Mechanism of Action in NASH: Gemcabene has both liver- and cardio-protective properties

Gemphire's decision to move forward with development of gemcabene in NASH is based on the strong mechanistic rationale for the compound to target the pathology of the disease. It has the potential to add complementary mechanisms

that lower both liver TG (fat) and inflammation, which are believed to be important for preventing the progression to liver fibrosis, particularly for diabetic and obese patients, who represent a large portion of the NASH population. It has been shown that obesity and diabetes can reduce a patient's ability to remove atherogenic lipid particles from the blood. NASH patients have been shown to have a particularly high burden of these atherogenic disease causing fat particles. Preclinical and clinical studies have shown significant lowering in plasma atherogenic particles, TG and CRP (a measure of inflammation) in subjects given oral, once-daily gemcabene. Additionally, in an animal model of NASH, gemcabene oral administration demonstrated the ability to reduce the extent of inflammation, hepatocyte (liver cell) ballooning and fibrosis. In a clinical trial in obese non-diabetic subjects, gemcabene administration resulted in a doubling of the mean increase in glucose disposal rate compared to placebo suggesting potential effects on insulin sensitivity. Thus, gemcabene has been shown to ameliorate many abnormalities known to exist in NASH patients. Moreover, gemcabene's demonstrated efficacy in preclinical NASH models supports its potential utility in NASH, a disorder characterized by excess fat accumulation and inflammation of the liver.

Gemcabene's clean safety profile confers an important competitive advantage for both adult and pediatric NASH/NALFD

Gemphire has compiled an expansive data set on gemcabene from nearly 1100 subjects across 23 completed trials. The drug has been well tolerated and has not shown any liver toxicities at doses from 150 mg to 900 mg daily for up to 12 weeks. Gemcabene has also shown a low likelihood for drug-drug interactions, particularly with statins and metformin that are widely used in diabetic and dyslipidemic patients, underlying conditions associated with NASH.

Method of Use patent covering Gemcabene's use in the treatment of NAFLD/NASH was issued further enhancing Gemphire's intellectual property protection

In conjunction with initiation of the Phase II exploratory pediatric NASH trial, Gemphire announced the issuance of Patent No. US 9,849,104, "Treatment of NASH with Gemcabene", on December 26, 2017. The patent issued from one of two related patent applications that were filed in the U.S. and claim priority to an international PCT patent application filed on November 7, 2016. The company intends to prosecute related applications throughout the world. For the U.S. patent applications, the USPTO has indicated that the disclosure constitutes multiple inventions, in which the "Treatment of NASH with Gemcabene" is the first of the inventions issued in a patent.

Gemcabene's mechanism of action and safety profile are highly differentiated from other clinical candidates

Gemphire's product candidate gemcabene is a first-in-class, once-daily, oral therapy that may be suitable for patients who are unable to achieve normal levels of LDL-C or triglycerides with currently approved therapies, primarily statins. Gemcabene's mechanism of action (MOA) is designed to enhance the clearance of very low-density lipoproteins (VLDLs) in the plasma and inhibition of the production of cholesterol and triglycerides in the liver. The combined effect of these mechanisms has been clinically observed to result in a reduction of plasma non-HDL-C, VLDL-C, LDL-C, apolipoprotein B and triglycerides. In addition, gemcabene has been shown to markedly lower C-reactive protein in humans and improve insulin sensitization. Gemcabene's MOA is liver-directed involving downregulation of hepatic apolipoprotein C-III (apoC-III) mRNA expression and decrease of plasma apoC-III levels. Gemcabene has also been shown to reduce liver sulfatase-2 mRNA levels, known to be elevated in diabetic and obese patients. Elevated sulfatase-2 is thought to reduce the effectiveness of the liver VLDL-remnant receptor (also known as Syndecan-1), that normally plays a role in removing triglyceride containing particles from the plasma. Gemcabene also reduces acetyl-CoA carboxylase (ACC1), CCR2/CCR5 receptor and TNF-α mRNA levels, markers thought to be involved in the progression of NASH/NAFLD. Gemcabene has demonstrated POC efficacy for NASH in the rodent STAM™ model developed at SMC Laboratories in Tokyo, Japan. Gemcabene has been tested as monotherapy and in combination with statins and other drugs in nearly 1100 subjects across 23 Phase 1 and Phase 2 clinical trials. Given this profile of efficacy across multiple pathological pathways, as well as evidence of safety and tolerability, particularly when used as an add-on to many other therapeutic drugs, gemcabene has attributes that support studies in humans for NASH.

Conference Call and Webcast

Gemphire management will hold a conference call and webcast with slides at 4:30 pm ET today to discuss its NAFLD/NASH clinical program. To join the call, please dial (844) 494-0188 (domestic) or (425) 278-9114 (international) and reference conference ID 8792866. Presentation slides can be accessed at https://edge.media-server.com/m6/p/p9997vdf. A webcast replay will be available on the News & Events section of the Gemphire website for all interested parties following the call and will be archived and available for 90 days.

About Gemphire

Gemphire is a clinical-stage biopharmaceutical company that is committed to helping patients with cardiometabolic disorders, including dyslipidemia and NASH. The Company is focused on providing new treatment options for cardiometabolic diseases through its complementary, convenient, cost-effective product candidate gemcabene as add-on to the standard of care, especially statins, that will benefit patients, physicians, and payors. Gemphire's Phase 2 clinical program is evaluating the efficacy and safety of gemcabene in hypercholesterolemia, including FH and ASCVD, SHTG and NASH/NAFLD. Two trials supporting hypercholesterolemia have been completed under NCT02722408 and NCT02634151. Gemphire has completed recruitment for a clinical trial for SHTG under NCT02944383, and previously initiated a trial for adult NASH. Please visit www.gemphire.com for more information.

Forward Looking Statements

Any statements in this press release about Gemphire's future expectations, plans and prospects, including statements about Gemphire's financial prospects, future operations and sufficiency of funds for future operations, clinical development of Gemphire's product candidate, expectations regarding future clinical trials, regulatory submissions and meetings and future expectations and plans and prospects for Gemphire, expectations for the future competitive environment for gemcabene, expectations regarding operating expenses and cash used in operations, and other statements containing the words "believes," "anticipates," "estimates," "expects," "intends," "plans," "predicts," "projects," "targets," "may," "potential," "will," "would," "could," "should," "continue," "scheduled" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the success and timing of Gemphire's regulatory submissions and pre-clinical and clinical trials; regulatory requirements or developments; changes to Gemphire's clinical trial designs and regulatory pathways; changes in Gemphire's capital resource requirements; the actions of Gemphire's competitors; Gemphire's ability to obtain additional financing; Gemphire's ability to successfully market and distribute its product candidate, if approved; Gemphire's ability to obtain and maintain its intellectual property protection; and other factors discussed in the "Risk Factors" section of Gemphire's Annual Report on Form 10-K for the year ended December 31, 2016, Gemphire's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 and in other filings Gemphire makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent Gemphire's views as of the date hereof. Gemphire anticipates that subsequent events and developments will cause Gemphire's views to change. However, while Gemphire may elect to update these forward-looking statements at some point in the future, Gemphire specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Gemphire's views as of any date subsequent to the date hereof.

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